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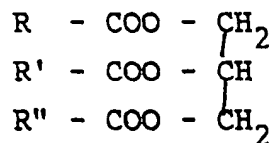
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(54) **Use of short chain fatty acid containing lipids to maintain gastrointestinal integrity and function in patients.**

(57) Use of short chain fatty acids for the preparation of a medicament for maintaining gastrointestinal integrity and function in conditions where normal short chain fatty acid substrates, provided by bacterial fermentation of carbohydrates, are inadequate due to the clinical condition of the patient. The medicaments can be provided either in enteral preparations or parenteral preparations.

The short chain fatty acids can be provided by hydrolysis of a structure such as:



wherein R-COO-, R'-COO-, and R''-COO- represent either the same or different short chain fatty acid residues.

The present invention relates to the use of short chain fatty acids containing lipids in clinical nutrition, specifically for the preparation of a medicament for maintaining gastrointestinal integrity and function in patients.

Lipids containing fatty acids having 2 to 6 carbon atoms, (short chain fatty acids - SCFA), are known to be produced in the gastrointestinal tract, in particular in the colon. Short chain fatty acids include acetic, propionic, butyric, isobutyric, pentanoic, isopentenoic and caproic. Typically, the short chain fatty acids are produced by bacterial fermentation. The substrates for the production of short chain fatty acids by bacterial fermentation are carbohydrates that are generally fibrous in nature.

The short chain fatty acids are used by the gastrointestinal mucosa as an energy substrate to maintain integrity and function. One method of providing gastrointestinal mucosa with short chain fatty acids is to utilise a dietary fiber which is converted by luminal microorganism digestion to fatty acids. Due to a variety of clinical reasons, the ability of the gastrointestinal mucosa to use short chain fatty acids as an energy source can be impaired.

When in the course of human disease, or therapy for disease, the bacterial flora of the gut is modified, reduced, or eliminated, its ability to provide short chain fatty acids as an energy substrate is impaired. There are a number of procedures, specifically with respect to hospitalised individuals that can greatly alter or eliminate the microflora of the gut. This can occur, for example, due to antibiotics, chemotherapy, or radiation. Furthermore, when the fiber intake of the patient is restricted, such as with some current elemental diets, there is no substrate for microorganism digestion even if the microflora are viable.

Because, in the above-identified conditions, short chain fatty acids cannot be used by the gastrointestinal tract as an energy substrate gastrointestinal integrity and function cannot be maintained.

The present invention provides a method for the use of short chain fatty acids containing lipids in clinical nutrition to maintain gastrointestinal integrity and function in conditions where normal short chain fatty acid (SCFA) substrates, provided by bacterial fermentation of carbohydrates, is inadequate due to the clinical condition of the patient. By providing the short chain fatty acid in a lipid form of free fatty acid, triglyceride, phospholipid, or cholesterol ester one is able to avoid the clinical defect and allow the gastrointestinal tract to continue to maintain its integrity and function. This is essential to good nutritional status, disease resistance, immune competence, and rapid recovery from the disease state.

The short chain fatty acids of the present invention can be provided either in enteral preparations administered by mouth, nasogastric, gastric, or jejunostomy tube. Additionally, the short chain fatty acids of the present invention can also be administered as a parenteral preparation by peripheral or central venous infusions. Additionally, the short chain fatty acids can be administered directly into the colon by enema.

The short chain fatty acids can be provided by hydrolysis of a triglyceride, diglyceride, or monoglyceride. For example, the short chain fatty acids can be provided by hydrolysis of a structure such as:



wherein R-COO-, R'-COO-, and R''-COO- represent either the same or different short chain fatty acid residues.

The short chain fatty acids can contain from two to six carbon atoms. Examples of the short chain fatty acids include acetic, propionic, butyric, and caproic. The short chain fatty acids can also include valeric and isovaleric acid.

In an embodiment, the short chain fatty acids are provided in compositions including a fat content having a range of from approximately 12% to about 45% of the total caloric content (19 grams to 53 grams per 500 ml) of the composition. In an embodiment of the present invention, the short chain fatty acids comprise approximately 10% to about 50% of the total caloric percent of the fat content of the composition (1.9 grams to 26.5 grams per 500 ml). The remainder of the lipids can be made up of medium chain triglycerides and long chain triglycerides.

Additional features and advantages of the present invention are described in, and will be apparent from, the detailed description of the presently preferred embodiments.

The short chain fatty acids can be administered with a nutritional source including carbohydrates, vitamins, minerals, pectins, amino acids and lipids.

The short chain fatty acids of the present invention can be administered either parenterally or enterally.

As an enteral preparation, the short chain fatty acid composition can be administered by mouth, nasogastric, gastric, or jejunostomy tube. As a parenteral preparation, the short chain fatty acids of the present invention can be administered by peripheral or central venous infusions. The short chain fatty acids can also be administered directly into the colon by enema.

5 By way of example, and not limitation, formulations of the present invention including short chain fatty acids will now be given.

#### Example 1

10 A medicament in the form of an enteral formulation for tube feeding or oral feeding can have the composition set forth below. The formulation provides a complete liquid nutrition formula suitable for various clinical indications. The composition provides complete and balanced nutrients and therefore can be used as a supplement or a total feeding. The formulation is isotonic and has a low renal solute load, making it an ideal standard tube-feeding formula.

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NUTRIENT COMPOSITION		per 250 ml AMOUNT
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	CALORIES	kcal	250
	PROTEIN	g	10
25	(% of calories)		(16%)
	CARBOHYDRATE	g	31.8
	(% of calories)		(51%)
30	FAT	g	9.5
	(% of calories)		(33%)
	SCFA	g	1.9
35	MCT	g	3.6
	LCT	g	4.0

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	<u>VITAMINS</u>		
	VITAMIN A	IU	940
5	VITAMIN D	IU	50
	VITAMIN E	IU	5
	VITAMIN K	mcg	31
10	VITAMIN C	mg	25
	THIAMINE (B <sub>1</sub> )	mg	0.38
	RIBOFLAVIN (B <sub>2</sub> )	mg	0.43
	NIACIN	mg	5
15	VITAMIN B <sub>6</sub>	mg	0.75
	FOLIC ACID	mcg	100
	PANTOTHENIC ACID	mg	2.5
20	VITAMIN B <sub>12</sub>	mcg	1.5
	BIOTIN	mcg	75
	CHOLINE	mg	110
25	<u>MINERALS</u>		
	SODIUM	mg	125
	POTASSIUM	mg	313
	CHLORIDE	mg	250
30	CALCIUM	mg	125
	PHOSPHORUS	mg	125
	MAGNESIUM	mg	62.5
35	IRON	mg	2.3
	IODINE	mcg	19
	COPPER	mg	0.25
40	ZINC	mg	2.5
	MANGANESE	mg	0.5

#### 45 Example 2

A medicament formulated for tube feeding or oral feeding, pursuant to the present invention, can have the formulation set forth below. The formulation provides a nutritionally complete and high caloric liquid nutrition composition, indicated when increased calories are needed in a concentrated form. Low osmolality  
50 allows the formulation to be used as a tube feeding.

NUTRIENT COMPOSITION		per 250 ml
		AMOUNT
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	CALORIES	kcal 375
	PROTEIN	g 15
10	(% of calories)	(16%)
	CARBOHYDRATE	g 42.5
	(% of calories)	(45%)
	FAT	g 16.9
15	(% of calories)	(39%)
	SCFA	g 5.0
	MCT	g 5.9
	LCT	g 6.0
20	<u>VITAMINS</u>	
	VITAMIN A	IU 1400
	VITAMIN D	IU 75
25	VITAMIN E	IU 7.5
	VITAMIN K	mcg 47
	VITAMIN C	mg 38
	THIAMINE (B <sub>1</sub> )	mg 0.56
30	RIBOFLAVIN (B <sub>2</sub> )	mg 0.64
	NIACIN	mg 7.5
	VITAMIN B <sub>6</sub>	mg 1.1
	FOLIC ACID	mcg 150
35	PANTOTHENIC ACID	mg 3.8
	VITAMIN B <sub>12</sub>	mcg 2.3
	BIOTIN	mcg 110
	CHOLINE	mg 170
40	<u>MINERALS</u>	
	SODIUM	mg 188
	POTASSIUM	mg 470
45	CHLORIDE	mg 375
	CALCIUM	mg 188
	PHOSPHORUS	mg 188
	MAGNESIUM	mg 94
50	IRON	mg 3.4
	IODINE	mcg 28

COPPER	mg	0.38
ZINC	mg	3.8
MANGANESE	mg	0.75

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Example 3

10 A medicament, an enteral formulation for tube feeding or oral feeding, pursuant to the present invention, can have the formulation set forth below. The formulation provides a complete and balanced enteral formula that can be used as a tube or oral feeding and is indicated for severe fluid restriction or extremely high caloric requirements.

15 NUTRIENT COMPOSITION per 250 ml  
AMOUNT

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CALORIES	kcal	500
PROTEIN	g	20
(% of calories)		(16%)
25 CARBOHYDRATE	g	49
(% of calories)		(39%)
FAT	g	26.5
30 (% of calories)		(45%)
SCFA	g	13.0
MCT	g	6.0
35 LCT	g	7.5

VITAMINS

VITAMIN A	IU	1900
40 VITAMIN D	IU	100
VITAMIN E	IU	10
VITAMIN K	mcg	63
VITAMIN C	mg	50
45 THIAMINE (B <sub>1</sub> )	mg	0.75
RIBOFLAVIN (B <sub>2</sub> )	mg	0.85

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	NIACIN	mg	10
	VITAMIN B <sub>6</sub>	mg	1.5
5	FOLIC ACID	mcg	200
	PANTOTHENIC ACID	mg	5
	VITAMIN B <sub>12</sub>	mcg	3
10	BIOTIN	mcg	150
	CHOLINE	mg	230
	<u>MINERALS</u>		
	SODIUM	mg	250
15	POTASSIUM	mg	625
	CHLORIDE	mg	500
	CALCIUM	mg	250
20	PHOSPHORUS	mg	250
	MAGNESIUM	mg	125
	IRON	mg	4.5
25	IODINE	mcg	38
	COPPER	mg	0.5
	ZINC	mg	5
30	MANGANESE	mg	1

Example 4

35 A liquid, isotonic, medicament including short chain fatty acids, pursuant to the present invention, can have the following composition. The composition provides an easily digested formula.

40 NUTRIENT COMPOSITION per 250 ml  
AMOUNT

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45	CALORIES	kcal	500
	PROTEIN	g	20.0
	CARBOHYDRATE	g	63.5
50	FAT***	g	19.5
	SCFA	g	6.5
	MCT	g	7.0

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	LCT	g	6.0
	<u>VITAMINS</u>		
5	VITAMIN A	IU	1875
	VITAMIN D	IU	100
	VITAMIN E	IU	10
	VITAMIN K	mcg	62.5
10	VITAMIN C	mg	50
	THIAMINE (B <sub>1</sub> )	mg	0.75
	RIBOFLAVIN (B <sub>2</sub> )	mg	0.85
15	NIACIN	mg	10
	VITAMIN B <sub>6</sub>	mg	1.5
	FOLIC ACID	mcg	200
20	PANTOTHENIC ACID	mg	5
	VITAMIN B <sub>12</sub>	mcg	3
	BIOTIN	mcg	150
	CHOLINE	mg	225
25	<u>MINERALS</u>		
	SODIUM	mg	250
	POTASSIUM	mg	625
30	CHLORIDE	mg	500
	CALCIUM	mg	300
	PHOSPHORUS	mg	250
35	MAGNESIUM	mg	150
	IRON	mg	4.5
	IODINE	mcg	37.5
	COPPER	mg	0.5
40	ZINC	mg	5.0
	MANGANESE	mg	1.0

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**Claims**

1. Use of short chain fatty acids for the preparation of a medicament for maintaining gastrointestinal integrity and function in patients.
2. Use according to claim 1 in which the fatty acid is at least one of acetic, propionic, butyric, caproic, valeric or isovaleric acid.
3. Use according to claim 1 or claim 2 in which the medicament is adapted for enteral or parenteral administration.
4. Use according to any preceding claim wherein short chain fatty acids supply 1.2 to 22.5% of the total caloric content of the medicament.

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5. Use according to any preceding claim wherein the medicament is in the form of an emulsion.
6. Use according to any preceding claim wherein the medicament comprises at least one mono-, di- or triglyceride which yields short chain fatty acids on hydrolysis.
- 5 7. Use according to any preceding claim wherein the medicament comprises a lipid source supplying short chain fatty acids which provides 12 to 45% of the caloric content of the medicament.
8. Use according to any preceding claim wherein the medicament contains at least one of a protein  
10 source, a carbohydrate source, a mineral source, a vitamin source, a medium chain triglyceride (MCT) source and a long chain triglyceride (LCT) source.
9. Use according to any preceding claim in which short chain fatty acids represent 10 to 50% of the caloric content of the lipids present in the medicament.

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